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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/671,687	09/28/2000	David Wallach	WALLACH=25	7238

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EXAMINER

LAMBERTSON, DAVID A

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/671,687	<b>Applicant(s)</b> WALLACH ET AL.	
	<b>Examiner</b> David A. Lambertson	<b>Art Unit</b> 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 2-4, 20-24 and 38-48 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2, 4, 20-24 and 38-43 is/are rejected.
- 7) ☒ Claim(s) 3 and 44-48 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

Art Unit: 1636

### DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed March 3, 2004.

Amendments were made to the claims.

Claims 2-4, 20-24 and 28-48 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, mailed November 3, 2003, that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-4, 20-24 and 38-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated protein capable of binding to TRAF2 and having an amino acid sequence having at least 90% homology to SEQ ID NO: 3, does not reasonably provide enablement for fragments of variants having as little as 90% homology to SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. **This rejection is maintained for the reasons set forth in the previous Office Action.**

***Response to Arguments Concerning Claim Rejections - 35 USC § 112***

Applicant's arguments filed March 3, 2004 have been fully considered but they are not persuasive. Applicant provides the following grounds of traversal in relation to the outstanding rejection set forth above:

1. Applicant alleges that the possibility that there may be a functional domain that has absolutely no homology to SEQ ID NO: 3 and folds and functions independently of the rest of the protein is irrelevant. Applicant's basis for this statement is that the remainder of the protein outside of this domain would necessarily be 100% identical to SEQ ID NO: 3. Applicant then states that this would mean that "the variant has a domain that clearly binds to TRAF2 regardless of whether or not there is an independently functioning domain which has no homology to SEQ ID NO: 3, and can, for some unknown reason also fortuitously bind to TRAF2." Applicant further states that this is similar to a fusion protein comprising SEQ ID NO: 3, and that such a claim was found allowable (see for example page 8-10 of Applicant's Remarks).
2. Applicant asserts that one of ordinary skill in the art would necessarily take a fragment of a variant having 90% homology to SEQ ID NO: 3 form an area of high sequence similarity, rather than an area of low sequence similarity (see for example page 10, first full paragraph of Applicant's remarks).

Applicant's arguments have been fully considered but are not convincing for the following reasons:

1. The point of the rejection is that a *fragment* of a variant having as little as 90% homology to SEQ ID NO: 3 could be made that has absolutely no identity or similarity to SEQ ID NO: 3.

Art Unit: 1636

Specifically, claim 2, part (C) reads on a fragment of a variant of SEQ ID NO: 3, wherein said variant has as little as 90% identity with SEQ ID NO: 3. It is noted that it is not necessary in the claims, as written, that the fragment have any homology whatsoever to SEQ ID NO: 3. As presented in the original rejection, a protein having 90% homology to SEQ ID NO: 3 can have as many as 95 amino acid changes. As claimed, all of these changes can be consecutive; for example, the first 95 amino acids of SEQ ID NO: 3 can be completely changed into any 1 of the  $3.96 \times 10^{123}$  ( $20^{95}$ ) possibilities allowed, and that fragment can be “chosen” as having the ability to bind to TRAF2. Thus, Applicant has claimed  $3.96 \times 10^{123}$  polypeptide fragments of 95 amino acids in length (or fewer than 95 amino acids in length), none of which have been described in the instant specification, and most of which will have no structural relationship to SEQ ID NO: 3 in any sense. In an even more egregious situation, one out of every two amino acids can be changed, giving a 190 amino acid long polypeptide having very low homology to SEQ ID NO: 3 (approximately 50%), and therefore virtually no relative structural similarity with SEQ ID NO: 3. Applicant’s assertion that this is irrelevant is unsubstantiated, based on this explanation. Applicant’s statement that “the variant has a domain that clearly binds to TRAF2 regardless of whether or not there is an independently functioning domain which has no homology to SEQ ID NO: 3, and can, for some unknown reason also fortuitously bind to TRAF2,” is what is irrelevant, because a full length polypeptide is not the subject of the claimed invention that is being rejected. What is being rejected is any fragment of a variant having as little as 90% homology to SEQ ID NO: 3, where the fragment has no homology requirement with regard to SEQ ID NO: 3. Thus, the portion that binds to TRAF2 is *not* a domain of the variant that has any homology to SEQ ID NO: 3, but rather a random polypeptide of up to 95 amino acids long

Art Unit: 1636

(or 190 amino acids long, if only every other amino acid is changed, etc.). Similarly, this is not the same situation as a fusion protein, because the claim is directed to a fragment of the protein, and not the collective protein (as would be the case with a fusion protein).

2. While one of ordinary skill in the art *might* take a fragment of a variant having 90% homology to SEQ ID NO: 3 from an area of high sequence similarity, rather than an area of low sequence similarity, this is not a certainty, nor is it reflected in the claim. The fact of the matter is that the claim does indeed read on the  $3.96 \times 10^{123}$  polypeptide fragments of 95 (or fewer) amino acids in length, as well as other polypeptides with virtually no homology to SEQ ID NO:

3. However, these polypeptides are not described in the specification, nor would one of skill in the art be able to reasonably make those polypeptides that necessarily bind to TRAF2 without undue and unpredictable trial and error experimentation. It is again reiterated that the ability to identify is not the ability to make. Certainly, randomly searching through  $3.96 \times 10^{123}$  polypeptide fragments of 95 (or fewer) amino acids in length cannot be considered a reasonable amount of experimentation, especially in light of the fact that there is absolutely no way to predict which, if any, of these polypeptides has the capacity to bind to TRAF2. If it is Applicant's contention that they would not select an area of low (or no) homology with regard to polypeptide fragments of variants of SEQ ID NO: 3, this should be reflected in the claim. In the absence of a limitation reflecting this, the claim must be read as broadly as within reason, and Applicant is clearly not enabled for the full scope of fragments that are being claimed.

In conclusion, Applicant is clearly not enabled for the  $3.96 \times 10^{123}$  polypeptide fragments of 95 (or fewer) amino acids in length that are (at least) being claimed, as well as numerous other polypeptide fragments having virtually no homology to SEQ ID NO: 3, because one cannot

Art Unit: 1636

make the fragments therein that are necessarily capable of binding to TRAF2 without undue and unpredictable trial and error experimentation. Applicant's arguments regarding the high degree of homology along the remainder of the polypeptide are irrelevant because that portion of the protein is not contained within the *fragment* that is being claimed. Furthermore, Applicant's claim that the ordinary skilled artisan would necessarily take a fragment of a variant having 90% homology to SEQ ID NO: 3 form an area of high sequence similarity, rather than an area of low sequence similarity is moot because such the argument odes not reflect what is being claimed. As such, the enablement rejection is maintained for the reasons set forth in the previous Office Action and in the response to Applicant's arguments indicated above.

*Allowable Subject Matter*

Claims 3 and 44-48 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

Art Unit: 1636


CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.  
AU 1636



**JAMES KETTER**  
**PRIMARY EXAMINER**